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Meta Analysis

The Association Between Matrix Metalloproteinases-9–1562 C/T Polymorphism and Lung Cancer Susceptibility: A Systematic Review and Meta-Analysis

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Abstract

Introduction: Matrix metalloproteinases (MMPs) are a family of zinc dependent proteinase. Several studies have reported the association between the single nucleotide polymorphisms(C/T) -1562 in the MMP-9 promoter and the risk of cancer. In this study we decided to carry out a comprehensive meta-analysis to obtain a reasonable result about the association between this polymorphism and the risk of lung cancer.

Materials and Methods: A complete literature review was conducted within the databases of ISI Web of Knowledge, google scholar and PubMed for studies on lung cancer published from 2002 to 2018. A meta-analysis was conducted which included more than 3000 case and control subjects. The pooled odds ratio (OR) and 95% confidence intervals (CI) were used for dominant, recessive and co-dominant MMP-9 genotypes to assess the strength of the association.

Results: Analysis indicated no significant association between MMP-9-1562C/T polymorphism and the risk of lung cancer, dominant model; [CT+TT/CC]: OR=0.972, 95% CI=0.811–1.164, recessive model [CC+CT/TT] OR= 1.027, 95% CI=0.651–1.618 and co-dominant model [TT/CC] OR=0.983, 95% CI=0.550–1.755.

Conclusions: No association was observed between the MMP9-1562 C/T polymorphism and the incidence of lung cancer. Meta-analysis demonstrated that this polymorphism can't serve as a diagnostic marker for lung cancer.

Keywords: MMP-9, Lung Cancer, Polymorphism

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Introduction

Lung cancer is the most common malignancy and has been the most common cause of deaths from cancer in the past few decades.[1] A total of 1.8 million new cases were estimated in 2012 which includes 12.9% of all newly diagnosed cancers. The patient's five-year survival rate is much lower than that of other cancers (17.8%).[2,3] The most important risk factors of lung cancer include tobacco smoking and aging. In addition to the mentioned factors, genetic background plays an important role in the development of this disease.[4] Matrix metalloproteases (MMPs) are a large family of zinc dependent proteinases consisting of more than 26 members; they act based on digestion of extracellular matrix (ECM) and basement membrane components. Since the ECM acts as an anchorage for stabilization of cells, increased MMPs level are required for invasion and migration of cancer cells.[5,6] The MMPs also act on cleavage of cell adhesion molecules such as growth factors, cell surface receptors, chemokines/cytokines and they may regulate angiogenesis in cancer process through the activation of proangiogenic factors.[7-9] The MMP-9 (type IV collagenase) is one of the most important members of the metalloproteinase family which plays a role in degrading of both basement membrane components and collagen attachments around the cells. A cytosine (C) to thymine (T) base substitution at position -1562 in the upstream of the MMP-9 transcription initiation site (MMP-9–1562C/T) causes MMP-9 over expression.[10]

Several studies have reported that CT and TT genotypes of MMP-9–1562C/T polymorphisms are associated with the occurrence and progression of some cancers, including colon, breast and lung cancer.[11-13] In previous studies, a significant association was found between the T allele and occurrence of breast cancer in the Iranian population. It was also found that T allele increases the plasma MMP-9 levels in breast cancer patients.[14,15] On the other hand, there are reports about the association between the presence of MMP-9 promoter T allele and lower risk of lung cancer in the Spanish,[16] Turkish[17] and French populations.[18] Another study published by Chinese researchers did not suggest a relevant association between MMP-9–1562 C/T polymorphism and lung cancer.[19]